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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/522,716	03/10/2000	Edward P. Cohen	10464A	6035

7590 02/26/2004

ATT: IP PROSECUTION
HOWREY, SIMON, ARNOLD & WHITE, LLP
1299 PENNSYLVANIA AVENUE, N.W.
BOX NO. 34
WASHINGTON, DC 20004-2402

EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 02/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/522,716	COHEN, EDWARD P.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26 and 41-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,41,42,44,45 and 47-53* is/are rejected.

7)☐ Claim(s) *43 and 46* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed 10/14/2003 is acknowledged and entered into the record. Accordingly, claims 1-25, and 27-40 are cancelled without prejudice or disclaimer and claims 47-53 are newly added.

2. Claims 26, 41-53 are pending and examined on the merits.

Claim Rejections Maintained - 35 USC § 102

3. The rejection of claims 26, 41, 42, and 44-45 under 35 USC 102 (b) as being anticipated by Eisenbach *et al* is maintained for the reasons of record. Applicant argues that the cited reference does not teach each and every limitation of the claimed invention, specifically that the reference does not teach the transformation of a cell with DNA from a tumor. Applicant's arguments have been carefully considered but are not found persuasive because the term "genomic DNA" as recited in the instantly claimed invention has not been adequately defined in the specification, therefore because the MHC determinants used by Eisenbach *et al* where derived from the genome of a tumor cell of a mouse, hence "genomic DNA", one of skill in the art would have anticipated that the limitation of transfecting an antigen presenting cell with a genomic DNA was also encompassed within the scope of the claims, wherein the genomic DNA used by Eisenbach *et al* was the DNA encoding the MHC determinant being transfected into the cell.

Claim Rejections Maintained - 35 USC § 102

4. The rejection of claims 26,41-42, and 44-45 under 35 USC 102(e) as being anticipated by Eisenbach *et al* is maintained for the reasons of record. Applicant's

arguments are essentially the same as that made for the 35 USC 102(b) rejection, *supra*. Applicant's arguments have been carefully considered but are not found persuasive because the term "genomic DNA" as recited in the instantly claimed invention has not been adequately defined in the specification, therefore because the MHC determinants used by Eisenbach *et al* where derived from the genome of a tumor cell of a mouse, hence "genomic DNA", one of skill in the art would have anticipated that the limitation of transfecting an antigen presenting cell with a genomic DNA was also encompassed within the scope of the claims, wherein the genomic DNA used by Eisenbach *et al* was the DNA encoding the MHC determinant being transfected into the cell.

New Arguments

Claim Rejections - 35 USC § 112, 1st paragraph

5. Claims 47-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a tumor comprsing the administration of an antigen presenting cell comprising an MHC I/II class determinant that is syngeneic and am MHC class I/II class determinant that is allogeneic, does not reasonably provide enablement for a method of preventing the recurrence of a tumor comprising the administration of an antigen presenting cell comprising an MHC I/II class determinant that is syngeneic and am MHC class I/II class determinant that is allogeneic. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims of the instant invention are drawn to a method of preventing a tumor in an animal comprising the administration of an antigen presenting cell expressing a syngeneic MHC I or II molecule, an allogeneic MHC I or II molecule, a cytokine, and genomic DNA isolated from tumor cells of said animal. The specification discloses the transformation of an LM cell (a fibroblast cell line) expressing an MHC I molecule H-2^K with a vector encoding an IL-2 molecule, thereby generating the new cell line LM-IL-2. The specification also details the further transformation of cell, LM-IL-2, with an additional MHC class I molecule, H-$2K^b$. And lastly, the specification teaches the transformation of LM-IL-ZK^b with genomic DNA isolated from the tumor of the animal, and the subsequent administration and inhibition of tumor growth in the animal. However, nowhere in the specification does it teach a method of administering to an animal a semi-allogeneic antigen presenting cell for a method of preventing a tumor recurrence in an animal.

In general, the treatment of cancer is at most unpredictable as underscored by Gura (Science, v278, 1997, pp.1041-1042) who discusses the potential shortcomings of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated with clonogenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041, 1st column) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive. Further, Bellone *et al.* (Immunology Today, v20

(10), 1999, pp.457-462) summarize the current state of the art of peptide immunotherapy including clinical trials where "there is usually a poor correlation between induction of specific T-cells and the clinical responses" (page 457, 2nd column). Bellone *et al.* teach the disadvantages of peptide cancer immunotherapy in that (1) there is no direct evidence for a role in tumor rejection, (2) the therapy is applicable to few patients, (3) risk of generating tumor escape mutants, and (4) risk of autoimmune reactions (page 461, Box 1). All of this underscores the criticality of providing workable examples which is not disclosed in the specification, particularly in an unpredictable art, such as cancer prevention.

Furthermore, reasonable guidance with respect to preventing any cancer relies on quantitative analysis from defined populations which have been successfully pre-screened and are predisposed to particular types of cancer. This type of data might be derived from widespread genetic analysis, cancer clusters, or family histories. The essential element towards the validation of a preventive therapeutic is the ability to test the drug on subjects monitored in advance of clinical cancer and *link* those results with subsequent histological confirmation of the presence or absence of disease. This irrefutable link between antecedent drug and subsequent knowledge of the prevention of the disease is the essence of a valid preventive agent. Further, a preventive administration also must assume that the therapeutic will be safe and tolerable for anyone susceptible to the disease. Take for example the antibody-based therapies, of which have shown some promising efficacy in the therapy of cancer, (Weiner L.M., Seminars Oncology, Vol. 26, No. 4, Suppl 12, pages 41-50, 1999), a recent review of

such therapies did not indicate nor suggest that such therapies would be successful in the prevention of cancer.

Therefore, given the unpredictable nature of cancer treatment in general, one of skill in the art would be forced to experiment to determine the means to practice the full scope of the instant invention because the treatment of cancer, as stated earlier is already unpredictable and difficult.

All other rejections are withdrawn in view of the applicant's amendments and arguments thereto as set forth in the Paper submitted 10/14/2003.

Conclusion

6. Claims 26, 41-42, 47-53 are rejected, claims 43 and 46 are objected to for depending on rejected claims. Therefore, no claim is allowable.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
January 7, 2004